AMENDMENTS

In the Specification:

Please replace the paragraph beginning at page 31, line 17, with the following amended paragraph.

A construct of *rad3*, in which the 794 amino acids between aa 1477 and aa 2271 (including kinase domain) were replaced with a *ura4+* gene, was created using the methodology describerd in Barbet *et al.* (1992). A linear fragment of this was used to transform sp011 to uracil prototropy and single copy integration at the *rad3* locus was checked by Southern blotting. To create the site specific kinase null mutations, a C-terminsl 3.01 kb *bam*HI-*sal*I fragment of *rad3* was mutated with either (A: GTTTTCGCCATGGCGCGCTCCCAAACCCAA (SEQ ID NO: 5), B: TTCATCAAACAATATCTTTTCGCCATGGCG (SEQ ID NO: 6), or C: CAAAAAGACAGTTGAATTCGACATGGATAG (SEQ ID NO: 7)) in order to introduce either the D2230A, N2235K or D2249E mutations into the kinase domain. Analgous changes have previously been used in the analysis of P13 kinase *vps34* of *S. cerevisiae* (Schu *et al.* 1993). These fragments were then used to transform the *rad3.d* null mutant and gene replacements selected by their ability to grow on FOA containing media (Grimm *et al.* 1988). All strains were checked by Southern blotting. Full length expression constructs of *rad3.D2230A* were created in pREP1 and pREP41 (Maundrell, 1990) by standard subcloning following introduction of an *NdeI* site at the ATG and deletion of three internal *NdeI* sites.

Please replace the paragraph beginning at page 32, line 6, with the following amended paragraph.

To isolate an appropriate probe for identifying cDNAs corresponding to a human *rad3* homologue, degenerate oligonucleotides were designed against the amino acids LGLGDRH (5' oligo; oDH18)(SEQ ID NO: 13) and HVDF[D/N]C (3' oligo; oDH-16)(SEQ ID NO: 14) or Rad3/Esr1p. Inosine was incorporated at positions of four-fold degeneracy, and primers were tailed with *Bam*HI (oDH18) and *Eco*RI (oDH16) to facilitate cloning. DNA sequencen analysis of the ~100 bp PCR product obtained from amplification of peripheral blood leukocyte cDNA demonstrated significant similarity to *MEC1/rad3*. This sequence was used to synthesize a non-degenerate primer (oDH-23;

GACGCAGAATTCACCAGTCAAAGAATCAAAGAG (SEQ ID NO: 8)) for PCR with an additional degenerate primer (oDH17) designed against the amino acid sequence KFPP[I/V][L/F]Y[Q/E]WF (SEQ ID NO: 12) of Rad3/Esr1p. The 174 bp product of this reaction was used directly to screen a macrophage cDNA library. Four positive clones were isolated (the largest approximately 3 kb).

Please replace the paragraph beginning at page 33, line 8, with the following amended paragraph.

Northern blot hybridisation : a 1.3 kb PCR product was amplified in the presence of ^{32}P-dCTP using primers 279-3 (TGGATGATGA CAGCTGTGTC (SEQ ID NO:9)) and 279-6 (TGTAGTCGCT GCTCAATGTC (SEQ ID NO:10)). A nylon mambrane containing 2μg of size-fractionated poly A+ RNA from a variety of human tissue sources (Clontech Laboratories) was probed as recommended by the manufacturer except that the final wash was performed at 55°C rather than 50°C to minimize the possibility of cross-hybridization to related sequences.

Please replace the paragraph beginning at page 33, line 16, with the following amended paragraph.

We mapped the ATR gene to chromosome 3 by a combination of fluorescent in situ hybridisation and polymerase chain reaction (PCR) based assays. FISH analysis using a cDNA clone identified the ATR gene on chromosome 3. Two primers (oATR23: GACGCAGAATTCACCAGTCAAAGAATCAAAGAG (SEQ ID NO: 8) and oATR26: TGGTTTCTGAGAACATTCCCTGA (SEQ ID NO:11)) which amplify a 257 bp fragment of the ATR gene were used on DNA derived from human/rodent somatic cell hybrids containing various human chromosome panels available from the NIGMS Human Genetic Mutant Cell Repository (Drwinga *et al.* 1993). PCR with the same primers was used to sub-localise ATR to a specific region on chromosome 3. The templates for these amplifications consisted of DNA samples from patients with truncations along chromosome 3 (Leach *et al.* 1994).